INTERACTIONS AND COEXISTENCE OF SEROTONIN AND NEUROPEPTIDES IN SPINAL AUTONOMIC SYSTEMS. C. J. Helke and L. Yang. Dept. of Pharmacology and Neuroscience Program, Uniformed Services University of the Health Sciences, Bethesda, MD 20814 USA.

Serotonin (5-HT), substance P (SP), neurokinin A (NKA) and thyrotropin-releasing hormone (TRH) coexist in the ventral medullary neurons which project to the intermediolateral cell column (IML) of the thoracic spinal cord. Studies are underway to determine whether 5-HT, SP, NKA and TRH are released from the nerve terminals of the IML, interact with each other and thus regulate the activity of the sympathetic nervous system.

The release of 5-HT, SP and NKA from the microdissected intermediate area (includes the IML) of the rat thoracic spinal cord was investigated using an *in vitro* superfusion system. Potassium depolarization induced extracellular Ca^{2+}-dependent differential release of [^{3}H]5-HT, endogenous SP and endogenous NKA from the intermediate area. The release of [^{3}H]5-HT was induced by lower concentrations of K^+ while the release of SP and NKA required higher K^+ concentrations. The evoked release of [^{3}H]5-HT was regulated by 5-HT and presynaptic 5-HT_{1B} receptors. The basal release of [^{3}H]5-HT was regulated by SP and NK_1 agonists acting through NK_1 receptors. The K^+-stimulated release of SP from the intermediate area, at least partly, comes from serotonergic nerve terminals as serotoninergic neurotoxin treatment decreased the SP content and the absolute amount of SP released. However, the release of SP was not under the influence of endogenous 5-HT because 5-HT, 5-HT_{1B} and 5-HT_3 agonists failed to change the percentage of fractional release of SP. It is possible that the release of SP is regulated by presynaptic NK_1 receptors as a NK_1 receptor antagonist (GR82334) dose-dependently increased the K^+-stimulated release of SP. Neither NKA, an NK_2 agonist (GR64349), nor a TRH analog (MK-771) altered the release of [^{3}H]5-HT or SP.

These data demonstrate that coexisting 5-HT and neuropeptides in the intermediate area are differentially released, and that the release of one neurochemical can be regulated by presynaptic inhibitory autoreceptors as well as the actions of other coexisting neurochemicals. The role of these neurochemical interactions on the spinal regulation of the sympathetic nervous system remains to be determined.
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